Attorney Docket No. **IB-1888**
Declaration dated 08/05/09

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being transmitted to the US Patent & Trademark Office via the Office Electronic Filing System at the date and time shown below.

Dated: 09/03/2009 7:00pm EDT By: /Michelle Chew Wong/

NAME: Michelle Chew Wong

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Ian G. Brown, et al.	Confirmation No:	6914
Serial No.:	10/809,269	Group No.:	1657
Filed:	03/24/2004	Examiner:	William H Beisner
Title:	Biosensor Employing Large Patterned Arrays of Cells on CCD Chips		

DECLARATION OF DR. ELEANOR A. BLAKELY

1. My name is Eleanor A. Blakely, Ph.D. I am a biophysicist. I have approximately 36 years of experience in the fields of biophysics and radiation biology. My curriculum vitae is attached.

2. I am a named inventor on the above cited application. I have read the presently pending claims 1-5 and 7-36 as currently amended. The presently pending claims cover the biosensor that I along with the other named inventors, invented and now claim.

3. I have also read the Office Action dated April 5, 2009, the "Office Action." I have also read the prior art cited by the Office in the Office Action, namely Kovacs et al., Lu et al., Frank et al., and Miyamoto et al. I submit this declaration to provide evidence on the record as to the nonobviousness of my claimed invention in response to the rejections made in the Office Action.

4. We demonstrated diamond-like carbon directed cell adhesion and patterning for the first time in "Growth of Large Patterned Arrays of Neurons using Plasma Methods", I.G. Brown, K.A. Bjornstad, E.A. Blakely, J.E. Galvin, O.R. Monteiro and S. Sangyuenyongpipat, Plasma Phys. Control. Fusion 45, 547-554 (2003); ***Invited Paper*** presented at the 11th International Congress on Plasma Physics, (ICPP'02), Sydney, Australia, July 15-19, 2002. None to very little

cell growth was observed where DLC was not patterned. This was an important advantage because this allowed us to contain the cell growth immediately over the CCD sensor in a patterned manner.

5. The use of DLC patterned films to pattern cell growth was not an advantage that flowed naturally from following a suggestion of the prior art. This was an unexpected result because it was never shown or suggested by any prior art to use patterned films such as DLC on a sensor to pattern cell growth. For example, Figures 1 and 2 in Luo et al. show that growth and viability of cells grown on DLC track closely the same rates of growth and viability of the controls grown on plastic. In Figure 4, for DLC there is some improved adhesion in the beginning but that advantage levels off by day 5. In contrast we show great variability in cells grown on DLC patterned surfaces versus the non-patterned surface as shown in Figure 6 of the specification. Thus, in my opinion, one can conclude that Luo et al provides no motivation to pattern DLC films to direct cell growth and can be seen as teaching away from the patterned films.

6. One goal was to keep the cells in close or direct contact with the underlying CCD array for electrostatic detection of the cells and their activity using the CCD array. Thus, we used a thin protective film of micron-range thickness as opposed to the cell culture containers taught by these four cited references which feature centimeter thickness. It also had not been shown prior that thin films could be used to protect the sensitive electronics in a CCD array and that cells would remain viable for long-term growth (upwards of days and weeks at a time).

7. Prior to this time, others had only contemplated photographing cells with CCD cameras and detecting their electrostatic activity using microelectrodes. Others who had tried to pattern neuronal growth had to often resort to practices such as impaling neurons to control or direct their growth. In contrast, the novel use of the CCD for electrostatic detection in combination with the ability to pattern cell growth allowed us to control cell growth and detect cellular activity passively through electrostatic detection. This allowed us to make a biosensor using neurons-- the coated CCDs with DLC feature millions of individual sensors that can record changes in electrical potential from individual neurons in real time while precisely mapping each neuron's activity within the neural network.

8. We previously attached a copy of a special press release (Exhibit A) which describes that this invention was also nominated and awarded an R&D 100 award by R&D100 Magazine for this technology. As the magazine states on its website, "The winning of an R&D 100 Award provides a mark of excellence known to industry, government, and academia as proof that the product is one of the most innovative ideas of the year." R&D Magazine has been presenting these awards to the top 100 innovative ideas and inventions annually since 1963.

9. Our team was also awarded special DARPA funding to develop this biosensor invention, and our proposal received high marks when we applied for this funding. Furthermore, the licensee of this technology has received continued DARPA funding for the development of this technology. This funding was received several years in a row, despite that the funding is usually only given once and not normally renewed.

10. In my opinion, the Examiner has not appreciated this invention is well-beyond taking pictures of cells using a CCD camera through a cell plate as suggested by Miyamoto. Making transparent films that can pattern cell growth on a CCD array and using the CCD array for electrostatic detection of cell growth and activity were not obvious uses or advantages that flowed from the prior art. As shown in the Berkeley Lab news release, others in the field have recognized the invention as being novel and innovative as "the first step in creating combined biological and electronic chip biosensors and implants that can provide networks of living, interconnected cells for testing drugs and sensing toxins for homeland security."

11. I have been warned that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. 1001) and may jeopardize the validity of the application or any patent issuing thereon. All statements made of my own knowledge are true and all statements made on information and belief are believed to be true.

SIGNED:

Eleanor A. Blakely 6 August 2009

Eleanor A. Blakely, Ph.D.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Blakely, Eleanor A.	Senior Staff Biophysicist

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of San Diego, San Diego,	B.A.	1969	Biology (Chem. Minor)
University of Illinois, Urbana, IL	M.S.	1971	Biophysics
University of Illinois, Urbana, IL	Ph.D.	1975	Physiology

A. Positions and Honors

Research and/or Professional Experience

1975-1989 Staff Biophysicist, Lawrence Berkeley Laboratory (LBL), Univ. of California at Berkeley
1988-1994 Member of the LBL-wide Technical Salary Committee
1988-1992 Deputy Leader, Radiat. Biol. & DNA Repair Group, Life Sci. Div., Cell & Molec. Biol., LBL
1988-2007 LBL Grievance Hearing Officer
1989-present Senior Staff Biophysicist, LBL, University of California
1991-present Faculty Affiliate Appointment, Department of Radiological Health Sciences, Colorado State University, Fort Collins, CO
1993-present Member of the LBL-wide Radioactive Drug Research Committee
1994-present Clinical Professor of Radiation Medicine (non-tenured), Loma Linda University, School of Medicine, Loma Linda, CA
2002-present Deputy Chair of Institutional Biosafety Committee

Professional Activities

Associate Editor, Space Power (1981-1991); Elected Officer (Biology Councilor), Radiation Research Society (1984-1987); Associate Editor, Radiation Research (1984-1988); Appointed Member, Diagnostic Radiology Study Section-Division of Research Grants, NIH (1987- 1991); Appointed Member, National Council on Radiation Protection and Measurements (NCRP) Scientific Committee #75 on "Guidance on Radiation Received in Space Activities" (1990-present); Appointed Member, NCRP Scientific Committee #1-7-Information Needed to Make Radiation Protection Recommendations for Travel Beyond Low-Earth Orbit (1996-present); Advisory Committee Member, IAEA (International Atomic Energy Agency) (1998, 2004); Elected to Council Membership, National Council on Radiation Protection and Measurements (2000-2012); Scientific Director, NASA Space Research Summer School, Brookhaven National Lab (2007 and 2008).

Awards

U.S. A.E.C. Special Fellowship in Radiat. Sci. & Protect., Dept. of Phys. & Biophys. Univ. of Illinois (1969-1972); .Robert Emerson Graduate Teaching Award, School of Life Sciences, University of Illinois (1974); Nominated for listing in American Men and Women in Science (1979); Lawrence Berkeley Laboratory Outstanding Performance Award (1992 and 2004); DOE Office of Science Outstanding Mentor Award (2002); Lawrence Berkeley Laboratory Technology Transfer Award (2004); RD100 award from R&D (Research & Development) Magazine as a member of a team that developed one of the 100 best new technologies in the year 2005 (2005).

B. Selected peer-reviewed publications (in chronological order), 1984-2009

Blakely, E.A., F.Q.H. Ngo, S.B. Curtis, and C.A. Tobias. Heavy-ion radiobiology: Cellular studies. *Adv. in Radiat. Biol.* 11, 295-389, 1984.

Blakely, E.A., P.Y. Chang, and L. Lommel. Cell-cycle-dependent recovery from heavy-ion damage. *Radiat. Res.* 104, S145-S157, 1985.

Blakely, E., R. Roots, P. Chang, L. Lommel, L. Craise, E. Goodwin, and E. Yee. Cell-cycle-dependent X-ray OER: Role of endogenous glutathione. *NCI Mono-Interact. of Rad.&Chemotherapy.* Vol 6, 217-223, 1988.

Chang, P.Y., C.A. Tobias, and **E.A. Blakely.** Protein synthesis modulates the biological effectiveness of the combined action of hyperthermia and high-LET radiation. *Radiat. Res.* 129, 272-280, 1992.

Blakely, E.A. Cell inactivation by heavy-charged particles. *Radiat.Environ. Biophys.* 31,181-196, 1992.

Blakely, E.A., I.K. Daftari, W.J. Meecham, L.C. Alonso, et al. Helium-ion-induced human cataractogenesis. *Adv. Space Res.*, Vol. 14, No. 10, pp. (10)501-(10)505, 1994.

Meecham, W.J., S.M. Kroll, D.H. Char, J.R. Castro and **E.A. Blakely.** Anterior segment complications after helium ion radiation therapy for uveal melanoma, I. Radiation cataract. *Arch.Ophthalmol.* 112,197-203,1994.

Goodwin, E.H., **E.A. Blakely,** and C.A. Tobias. Chromosomal damage and repair in G1-phase CHO cells exposed to charged particle beams. *Radiat. Res*, 138, 343-351, 1994.

Blakely, E. A. and R.J.M. Fry. Radiation protection in space, *Radiat. Environ. Biophys.* 34,129-131, 1995.

Blakely, E. A., Biological Beam Characterization. In Ion Beams in Tumor Therapy (Ed. U. Linz). Chapman & Hall, New York, pp. 63-72, 1995.

Daftari, I., D. Char, L.Verhey, J. Castro, P. Petti, W. Meecham, S. Kroll, **E.A. Blakely.** Anterior normal tissue sparing as a means of reducing complications of charged particle RT in uveal melanoma.*Int. J. Radiat. Oncol., Biol., Physics* 39, 989-996, 1997.

Castro, J., D. Char, P. Petti, I. Daftari, J. Quivey, R.P. Singh, **E.A. Blakely** and T. Phillips. 15 years experience with helium ion radiotherapy for uveal melanoma. *Int. J. Radiat. Oncol, Biol., Physics* 39, 997-1010, 1997.

Blakely, E.A., and A. Kronenberg. Heavy-ion radiobiology: New approaches to delineate mechanisms underlying enhanced biological effectiveness. *Radiat. Res.* 150, S126-S145, 1998.

Castro, J.R., P.L. Petti, **E.A.Blakely** and D.E. Linstadt. Particle Radiation Therapy. In Textbook of Radiation Oncology (Eds. Leibel and Phillips), W. B. Saunders Co., Philadelphia, PA, 1998 (1st Edition) and 2004 (2nd Edition)

Chang, P.Y., K.A. Bjornstad, E. Chang, M. McNamara, M.H. Barcellos-Hoff, S.P. Lin, G. Aragon, J.R. Polansky, G.M. Lui and **E.A. Blakely.** Particle irradiation induces FGF-2 expression in normal human lens cells. *Radiat. Res.* 154,477-484, 2000.

Blakely, E.A., K.A. Bjornstad, P.Y. Chang, et al. Growth and differentiation of human lens epithelial cells in vitro on matrix. *Invest. Ophthal.Vis Sci.* 41, 3898-3907, 2000.

Blakely, E.A. Biological Effects of Cosmic Radiation: Deterministic & Stochastic. *Health Phys.* 79,495-505, 2000.

McNamara, M.P.J., K.A. Bjornstad, P.Y. Chang, W. Chou, S.J. Lockett and **E.A. Blakely.** Modulation of lens cell adhesion molecules by particle beams. *Phys Med*, Vol. XVII, Suppl.1, pp. 247-248, 2001.

Blakely, E. A. New measurements for hadrontherapy and space radiation: Biology. *Phys Med,* Vol XVII, Suppl.1, pp. 50-58, 2001.

Blakely, E.A. and P. Y. Chang, Late effects from hadron therapy, *Radiotherapy & Oncology*, Suppl. 2, Vol. 73, S134-S140, 2004.

Chang, PY, KA Bjornstad, CJ Rosen, MP McNamara, R Mancini, LE Goldstein, LT Chylack, and **EA Blakely** Effects of iron ions, protons and xrays on human lens cell differentiation, *Radiat. Res.* 164(4): 531-539, 2005.

Chang, P.Y., K.A. Bjornstad, C.J. Rosen, S. Lin, **E.A. Blakely**. Particle radiation alters expression of matrix metalloproteases resulting in ECM remodeling in human lens cells. *Radiat Environ Biophys.* 46:187-194, 2007.

Blakely, E.A., P.Y. Chang. A Review of Ground-Based Heavy Ion Radiobiology Relevant to Space Radiation Risk Assessment: I. Cataracts and CNS Effects. *Adv in Space Res.* 40:1307-1319, 2007.

Blakely, E.A., P.Y. Chang. A Review of Ground-Based Heavy-ion Radiobiology Relevant to Space Radiation Risk Assessment. Part II: Cardiovascular and Immunological effects *Adv. Space Res. 40*:461-469, 2007.

Nikanjam M, **Blakely E.A.**, Bjornstad KA, Shu X, Budinger TF, Forte TM, Synthetic nano-low density lipoprotein as targeted drug delivery vehicle for glioblastoma multiforme, *Int J Pharm* 328(1):86-94, 2007.

Thompson AC, **Blakely EA**, Bjornstad KA, Chang, PY, Rosen, CJ, and Schwarz RI, A Synchrotron-Based X-ray Exposure Station for Radiation Biology Experiments, *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment, Volume 582, Issue 1, 11 November 2007, Pages 226-228, Proceedings of the 14th National Conference on Synchrotron Radiation Research - SRI 2007*

Levy RP, **Blakely EA,** Chu WT, Coutrakon GB, Hug EB, Kraft G, and Tsujii H, "The Current Status and Future Directions of Heavy Charged Particle Therapy in Medicine". Application of Accelerators in Research and Industry: Twentieth International Conference, Fort Worth (Texas), 10-15 August 2008, AIP Conference Proceedings Volume 1099, pp. 410-425 (2009).

Blakely E.A. and Chang, PY, Biology of Charged Particles, *The Cancer Journal, Vol. 15*(4):1-14, July/August 2009.